The Structure of EF-Tu-Kirromycin Complex: Implications for the Bacteriostatic and Bacteriocidal Action of the Antibiotic

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ABSTRACT

In the presence of the antibiotic, kirromycin, *Escherichia coli* elongation factor Tu (EF-Tu) adopts a conformation that remains bound to the ribosome, even after GTP hydrolysis, thus inhibiting further cycles of elongation. The three-dimensional structure of a complex between *E. coli* EF-Tu:GDP and kirromycin has been determined by X-ray diffraction analysis to a resolution of 2.2Å. The overall conformation of the complex is distinct from all previously observed EF-Tu structures, but is most similar to that of EF-Tu**-**GTP. Not only are the relative domain arrangements different from those observed in other complexes, but the antibiotic also alters the conformation of the Effector Loops I and II. Several kirromycin-resistant mutants have been identified and all sites map to the interface between Domains I and III [1,2]. A number of studies have suggested that the chromophoric end of kirromycin is involved in the interaction with EF-Tu**.** The present three-dimensional structure of EF-Tu-GDP-kirromycin explains all of the observed biochemical data. In its bacteriostatic mode, kirromycin alters the behavior of EF-Tu such that the activities normally elicited by EF-Ts, aminoacyl-tRNA and the ribosome are mimicked [3]. The new conformation of EF-Tu, in the presence of kirromycin, provides a structural explanation for all observed effects of kirromycin on each of the known EF-Tu complexes. The bacteriocidal mode is less well understood. It may be related to the observation that kirromycin promotes the formation of EF-Tu filaments [4], thereby removing all functional EF-Tu from the cell. An EF-Tu**-**GDP**-**kirromycin filament is observed in the crystal which may help to elucidate the molecular basis for the induced filament formation.

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This work was supported by NIH Grant GM26895 to Frances Jurnak.

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